Amendments to the Claims:

This listing of claims replaces all prior versions and listings of claims in the application:

Listing of Claims:

1-9. (Cancelled)

10. (Currently Amended) A method, comprising ~~for identifying, selecting or designing a chemical or biochemical species which is a modulator of RGS activity, RGS binding or RGS-Gα complex activity which comprised the steps~~:

(a) studying the interaction of one or more chemical or biochemical test species with ~~the~~ a three-dimensional ~~solution~~ structure of a polypeptide including at least a core region of a free ~~an~~ RGS4 protein ~~or a portion thereof~~; and

(b) selecting a potential modulator of an RGS protein from the one or more chemical or biochemical test species based on ~~a chemical or biochemical test species, which is predicted by its~~ the interaction of the one or more chemical or biochemical test species with the three-dimensional structure of the polypeptide ~~RGS4 to act as a modulator of an RGS protein to thereby identify, select or design the modulator~~.

11. (Currently Amended) The method of claim 10, wherein the free RGS4 protein has a Gα binding site, and the potential modulator is ~~identified,~~ selected ~~or designed~~ based on its ~~predicted~~ interaction with ~~a~~ the Gα binding site of ~~a~~ the free RGS4 protein.

12. (Currently Amended) The method of claim 10, wherein the free RGS4 protein has an allosteric binding site, and the potential modulator is ~~identified,~~ selected ~~or designed~~ based on its predicted interaction with ~~an~~ the allosteric binding site of ~~a~~ the free ~~RGS~~ RGS4 protein.

13. (Currently Amended) The method of claim 12, wherein the free RGS4 protein includes an α_1-α_2 region, and the allosteric binding site of the free RGS4 protein is located in the α_1-α_2 region of ~~a~~ the free RGS4 protein.

14. (Currently Amended) The method of claim 10, wherein the free RGS4 protein includes an α_6-α_7 region, and the potential modulator is ~~identified,~~ selected ~~or designed~~ based on its predicted interaction with the α_6-α_7 region of ~~a~~ the free RGS4 protein.

15. (Currently Amended) The method of claim 10, wherein the chemical or biochemical test species ~~are selected from~~ comprise small organic molecules.

16. (Currently Amended) The method of claim 10, further comprising ~~the steps of~~:

~~(a)~~ (c) obtaining the ~~selected test species~~ potential modulator; and

~~(b)~~ (d) assaying the ~~test species~~ potential modulator to measure its activity as a modulator of RGS activity, RGS binding or RGS-Gα complex activity.

17. (Cancelled).

18. (Currently Amended) A process, ~~for identifying a substance that inhibits RGS activity, RGS binding or RGS-Gα complex activity~~ comprising:

~~the step of~~ determining the interaction between a candidate species and ~~the structure of~~ a free RGS protein using ~~a representation of the~~ a three-dimensional ~~solution~~ structure of a polypeptide including at least a core region of a free RGS4 protein.

19. (Cancelled).

20. (Currently Amended) A method, ~~of identifying modulators of RGS activity, RGS binding or RGS4/Gα complex activity by rational drug design~~ comprising ~~the steps~~:

(a) designing a potential modulator that will form a ~~reversible or non-reversible~~ bond with one or more amino acids in the RGS4 Gα binding site of a free RGS4 protein based upon ~~the NMR~~ a three-dimensional structure ~~coordinates~~ of a polypeptide including at least a core region of the free ~~RGS~~ RGS4 protein;

(b) synthesizing or otherwise obtaining the potential modulator; and

(c) determining whether the potential modulator inhibits or promotes the activity of RGS or RGS4/G_α complex.

21. (Currently Amended) The method of claim 20, wherein ~~said~~ the RGS4 Gα binding site includes one or more amino acids, the potential modulator is designed to interact with one or more atoms of ~~said~~ the one or more amino acids in the RGS4 Gα binding site, and ~~wherein said~~ the one or more amino acids ~~is~~ are selected from the group consisting of D117, S118, ~~or~~ and R121.

22. (Currently Amended) The method of claim 20, wherein the RGS4 Gα binding site includes one or more amino acids, the potential modulator is designed to interact with one or more atoms of the one or more amino acids in the RGS4 Gα binding site, and the one or more amino acids are selected from the group consisting of S39, E41, N42, L113, D117, S118, R121, ~~or~~ and N82.

23. (Currently Amended) A method, ~~for identifying modulators of RGS activity, RGS binding or RGS4/Gα complex activity by rational drug design~~ comprising ~~the steps~~:

(a) designing a potential modulator that will form a ~~reversible or non-reversible~~ bond with one or more amino acids in the allosteric binding site in the α1-α2 region of ~~RGS~~ a free RGS4 protein based upon ~~the NMR~~ a three-dimensional structure ~~coordinates~~ of a polypeptide including at least a core region of the free RGS4 protein;

(b) synthesizing or otherwise obtaining the potential modulator; and

(c) determining whether the potential modulator inhibits or promotes the activity of RGS or RGS4/G_α complex.

24. (Currently Amended) The method of claim 23, wherein ~~said~~ the allosteric binding site includes one or more amino acids, the modulator is designed to interact with one or more atoms of ~~said~~ the one or more amino acids in the allosteric binding site, and ~~wherein said~~ the one or more ~~atoms~~ amino acids is selected from the group consisting of ~~RGS residues~~ V10, W13, L17, 120, H23, E24, C25 and T132.

25. (Cancelled).

26. (Currently Amended) A method of identifying modulators of RGS activity, RGS binding or RGS4/Gα complex activity by rational drug design, the method comprising ~~the steps~~:

(a) designing a potential modulator that will form a ~~reversible or non-reversible~~ bond with one or more amino acids in the α_6-α_7 region of a free RGS4 protein based upon a three-dimensional structure of a polypeptide including at least a core region of the free RGS4 protein;

(b) synthesizing or otherwise obtaining the potential modulator; and

(c) determining whether the potential modulator inhibits or promotes the activity of RGS or RGS4-G_α complex.

27. (Currently Amended) The method of claim 26, wherein an activity of the potential modulator ~~activity~~ is ~~assesses~~ assessed using an enzyme assay.

28. (Currently Amended) A method, ~~for identifying a potential modulator of RGS activity, RGS binding or RGS-Gα complex activity by rational drug design~~ comprising ~~the steps~~:

(a) providing a three dimensional structure of a polypeptide including at least a core region of a free RGS4 protein;

(b) employing the three dimensional structure of the polypeptide to select a potential antagonist or agonist of an RGS protein; and

(c) synthesizing or otherwise obtaining the potential antagonist or agonist.

[[30]]29. (Currently Amended) The method of claim 28, wherein the ~~three-dimensional structure of step (a) is that of~~ free RGS4 ~~as~~ is defined by the relative structural coordinates ~~of RGS4-core protein~~ according to Table 2, ± a root mean square deviation of not more than 1.5 Å from the conserved backbone atoms of the amino acids of ~~RGS4-core~~ the core region of the free RGS4 protein.

[[31]]30. (Cancelled).

[[32]]31. (Cancelled).

[[33]]32. (Cancelled).

[[34]]33. (Currently Amended) The method of claim 28, wherein ~~the~~ step (b) ~~of employing the three-dimensional structure to designing or select the potential inhibitor~~ comprises ~~the steps of: (1)~~ identifying a chemical or biochemical species ~~or fragments thereof capable of binding~~ that will bind to ~~an~~ the free RGS4 protein~~; and (2) assembling the identified chemical entities or fragments into a single molecule to provide the structure of a potential inhibitor~~.

[[35]]34. (Currently Amended) The method of claim ~~34~~33, wherein ~~in step (a)~~ the free RGS4 protein includes a Gα binding site, and the chemical or biochemical species ~~or fragments thereof capable of binding~~ is a protein that binds to the Gα binding site of ~~a free RGS-core is a protein~~ the free RGS4 protein.

[[36]]35. (Currently Amended) The method of claim ~~34~~33, wherein ~~in step (a)~~ the free RGS4 protein includes an α_1-α_2 region with an allosteric binding site, and the chemical or biochemical species ~~or fragments thereof capable of binding~~ binds to the allosteric binding site in the α_1-α_2 region of ~~a free RGS core protein are identified~~ the free RGS4 protein.

[[37]]36. (Currently Amended) The method of claim ~~34~~33, wherein ~~in step (a)~~ the RGS4 protein includes an α_6-α_7 region, and the chemical or biochemical species ~~or fragments thereof capable of binding~~ binds to the α_6-α_7 region of ~~a free RGS core protein are identified~~ the free RGS4 protein.

[[38]]37. (Currently Amended) The method of claim ~~34~~33, further comprising ~~the step of~~ testing the potential ~~inhibitor~~ antagonist or agonist ~~designed or selected in step (b)~~ as ~~an~~ a modulator of ~~an~~ RGS protein activity, RGS binding, or RGS-Gα complex activity.

[[39]]38. (Cancelled).

[[40]]39. (Cancelled).

[[41]]40. (Cancelled).

[[42]]41. (Cancelled).

[[43]]42. (Cancelled).

[[44]]43. (Cancelled).

[[45]]44. (Cancelled).

45. (New) The method of claim 10, wherein the free RGS4 protein is from a mammalian species.

46. (New) The method of claim 10, wherein the free RGS4 protein is from a human.

47. (New) The method of claim 10, wherein the potential modulator is an agonist of the RGS protein.

48. (New) The method of claim 10, wherein the potential modulator is an antagonist of the RGS protein.

49. (New) The method of claim 10, wherein the core region of the free RGS4 is defined by the relative structural coordinates of Table 2, ± a root mean square deviation of not more than 1.5 Å from the conserved backbone atoms of the amino acids of the core region of the free RGS4 protein.

50. (New) The method of claim 20, wherein the free RGS4 protein is from a mammalian species.

51. (New) The method of claim 20, wherein the free RGS4 protein is from a human.

52. (New) The method of claim 20, wherein the potential modulator is an agonist of the RGS protein.

53. (New) The method of claim 20, wherein the potential modulator is an antagonist of the RGS protein.

54. (New) The method of claim 20, wherein the core region of the free RGS4 is defined by the relative structural coordinates of Table 2, ± a root mean square deviation of not more than 1.5 Å from the conserved backbone atoms of the amino acids of the core region of the free RGS4 protein.

55. (New) The method of claim 23, wherein the free RGS4 protein is from a mammalian species.

56. (New) The method of claim 23, wherein the free RGS4 protein is from a human.

57. (New) The method of claim 23, wherein the potential modulator is an agonist of the RGS protein.

58. (New) The method of claim 23, wherein the potential modulator is an antagonist of the RGS protein.

59. (New) The method of claim 23, wherein the core region of the free RGS4 is defined by the relative structural coordinates of Table 2, ± a root mean square deviation of not more than 1.5 Å from the conserved backbone atoms of the amino acids of the core region of the free RGS4 protein.

60. (New) The method of claim 26, wherein the free RGS4 protein is from a mammalian species.

61. (New) The method of claim 26, wherein the free RGS4 protein is from a human.

62. (New) The method of claim 26, wherein the potential modulator is an agonist of the RGS protein.

63. (New) The method of claim 26, wherein the potential modulator is an antagonist of the RGS protein.

64. (New) The method of claim 26, wherein the core region of the free RGS4 is defined by the relative structural coordinates of Table 2, ± a root mean square deviation of not more than 1.5 Å from the conserved backbone atoms of the amino acids of the core region of the free RGS4 protein.

65. (New) The method of claim 28, wherein the free RGS4 protein is from a mammalian species.

66. (New) The method of claim 28, wherein the free RGS4 protein is from a human.